CLAIMS:

1. A method of inducing a dopaminergic neuronal fate in a neural stem cell or neural progenitor cell, the method comprising:
expressing *Nurr1* above basal levels within the cell, and
contacting the cell with one or more factors obtainable from a Type 1 astrocyte of the ventral mesencephalon, whereby dopaminergic neurons are produced.

2. A method according to claim 1 comprising contacting the cell with FGF8.

3. A method according to claim 1 comprising transforming a neural stem cell or neural progenitor cell with *Nurr1*.

4. A method according to any one of claims 1 to 3 comprising co-culturing the neural stem cell or neural progenitor cell with a Type 1 astrocyte of the ventral mesencephalon.

5. A method according to claim 4 wherein the Type 1 astrocyte is immortalized or is of an astrocyte cell line.

6. A method according to any one of the preceding claims wherein said cell is mitotic when it is contacted with said one or more factors.

7. A method according to any one of the preceding claims wherein said cell is additionally contacted with one or more agents selected from the group consisting of: basic fibroblast growth factor (bFGF), epidermal growth factor (EGF), an activator of the retinoid X receptor (RXR), and 9-cis retinol.

8. A method according to any one of the preceding claims wherein said cell is additionally contacted with a member of the FGF family of growth factors.

9. A method according to claim 8 wherein said cell is contacted with bFGF or EGF, and SR11237.

10. A method according to any one of the preceding claims wherein the neural stem cell or neural progenitor cell is pretreated with bFGF and/or EGF prior to contacting the cell with one or more factors obtainable from a Type 1 astrocyte of the ventral mesencephalon.

11. A method according to any one of the preceding claims further comprising formulating a dopaminergic neuron produced by the method into a composition comprising one or more additional components.

12. A method according to claim 11 wherein the composition comprises a pharmaceutically acceptable excipient.

13. A method according to claim 12 further comprising administering the composition to an individual.

14. A method according to claim 13 wherein the dopaminergic neuron is implanted into the brain of the individual.

15. A method according to claim 14 wherein the individual has Parkinson's disease.

16. A method according to any of claims 1 to 10 further comprising use of a dopaminergic neuron produced in accordance with the method in the manufacture of a medicament for

treatment of an individual.

17. A method according to claim 16 wherein the medicament is for implantation into the brain of the individual.

18. A method according to claim 17 wherein the individual has Parkinson's disease.

19. A dopaminergic neuron produced in accordance with any one of claims 1 to 10.

20. A composition comprising a dopaminergic neuron according to claim 19.

21. A composition according to claim 20 comprising one or more additional components.

22. Use of a dopaminergic neuron according to claim 19 in a method of screening for an agent for use in treatment of a neurodegenerative disease.

23. A method according to any one of claims 1 to 10 further comprising:

(i) treating a dopaminergic neuron with a toxin for said dopaminergic neuron;

(ii) separating the dopaminergic neuron from the toxin;

(iii) bringing the treated dopaminergic neuron into contact with a test agent or test agents;

(iv) determining the ability of the dopaminergic neuron to recover from the toxin;

(v) comparing said ability of the dopaminergic neuron to recover from the toxin with the ability of a dopaminergic neuron to recover from the toxin in the absence of contact with the test agent(s).

24. A method according to any one of claims 1 to 10 further comprising:

(i) treating a dopaminergic neuron with a toxin for the dopaminergic neuron in the presence of a test agent or test agents;

(ii) determining the ability of the dopaminergic neuron to tolerate the toxin;

(iii) comparing said ability of the dopaminergic neuron to tolerate the toxin with the ability of a dopaminergic neuron to tolerate the toxin in the absence of contact with the test agent(s).

25. A method according to claim 23 or claim 24 further comprising formulating an agent which improves ability of a dopaminergic neuron to recover from or tolerate a said toxin into a composition comprising one or more additional components.

26. A method according to claim 25 wherein said composition comprises a pharmaceutically acceptable excipient.

27. A method according to claim 26 further comprising administering said composition to an individual.

28. A method according to claim 27 wherein the individual has Parkinson's disease.

29. A method of screening for a receptor or receptors for the factor or factors which are obtainable from Type I astrocytes of the ventral mesencephalon and which induce a dopaminergic fate in neural stem or progenitor cells expressing Nurr-1 above basal levels, the method comprising comparing neural stem or progenitor cells with or without expression of Nurr-1

above basal levels within the neural stem or progenitor cells, to identify said receptor or receptors.

30. A method as in claim 29 which further comprises isolating and/or purifying and/or cloning said receptor or receptors.

31. A method as in claim 30 which further comprises using said receptor or receptors in a method of screening for said factors or factors obtainable from type I astrocytes of the ventral mesencephalon.

32. A method of screening for a factor or factors which, either alone or in combination, induce a dopaminergic fate in a neural stem or progenitor cell expressing *Nurr1* above basal levels, the method comprising:

(a) bringing Type 1 astrocyte molecules into contact with a neural stem cell or neural progenitor cell expressing *Nurr1* above basal levels, which contact may result in interaction between the Type 1 astrocyte molecules and the neural stem or progenitor cell; and

(b) determining interaction between the Type 1 astrocyte molecules and the stem or progenitor cell.

33. A method according to claim 22 which comprises comparing molecules of Type 1 astrocytes of the ventral mesencephalon with those of neural cells which are unable to induce a dopaminergic fate in neural stem or progenitor cells expressing *Nurr1* above basal levels.

34. A method of screening for a factor or factors which, either alone or in combination, induce a dopaminergic fate in a neural stem or progenitor cell expressing *Nurr1* above basal levels, the method comprising culturing a neural stem cell or

neural progenitor cell expressing *Nurr1* above basal levels in the presence of Type 1 astrocyte molecules and analyzing said cell for differentiation to a dopaminergic phenotype.

35. A method according to claim 34 which comprises comparing Type 1 astrocytes of the ventral mesencephalon with neural cells which are unable to induce a dopaminergic fate in neural stem or progenitor cells expressing *Nurr1* above basal levels.

36. A method according to claim 33 which comprises differential expression screening.

37. A method according to any one of claims 31 to 36 wherein a factor or factors able to induce a dopaminergic fate in a neural stem or progenitor cell expressing *Nurr1* above basal levels is or are provided in isolated and/or purified form.

38. A method according to any one of claims 31 to 37 wherein a factor or factors able to induce a dopaminergic fate in a neural stem or progenitor cell expressing *Nurr1* above basal levels is or are formulated into a composition comprising one or more additional components.

39. A method according to claim 38 wherein the composition comprises a neural stem or progenitor cell expressing *Nurr1* above basal levels.

40. A method according to claim 38 or claim 39 wherein the composition comprises a pharmaceutically acceptable excipient.

41. A method according to claim 40 further comprising administering the composition to an individual.

42. A method according to claim 41 wherein the composition is

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implanted into the brain of the individual.

43. A method according to claim 42 wherein the individual has Parkinson's disease.

44. A method according to any one of claims 31 to 37 further comprising use of a factor or factors able to induce a dopaminergic fate in a neural stem or progenitor cell expressing *Nurr1* above basal levels in the manufacture of a medicament for treatment of an individual.

45. A method according to claim 44 wherein the medicament comprises a neural stem or progenitor cell expressing *Nurr1* above basal levels.

46. A method according to claim 44 or claim 45 wherein the medicament is for implantation into the brain of the individual.

47. A method according to claim 46 wherein the individual has Parkinson's disease.

48. A method of screening for a substance which modulates the ability of Type 1 astrocytes of the ventral mesencephalon, or a molecule or molecules of such astrocytes, to induce a dopaminergic fate in neural stem or progenitor cells expressing *Nurr1* above basal levels, the method comprising:

(i) co-culturing Type 1 astrocytes with neural stem or progenitor cells which express *Nurr1* above basal levels in the presence of one or more test substances; or

(ii) bringing neural stem or progenitor cells which express *Nurr1* above basal levels into contact with one or more molecules of Type 1 astrocytes able to induce a dopaminergic phenotype in such cells, said contact occurring in the

presence of one or more test substances;
and

(iii) analysing the proportion of stem or progenitor cells which adopt a dopaminergic fate;

(iv) comparing the proportion of stem or progenitor cells which adopt a dopaminergic fate with the number of stem or progenitor cells which adopt a dopaminergic fate in comparable reaction medium and conditions in the absence of the test substance(s).

49. A method according to claim 48 wherein a substance which modulates the ability of Type 1 astrocytes of the ventral mesencephalon, or a molecule or molecules of such astrocytes, to induce a dopaminergic fate in neural stem or progenitor cells expressing *Nurr*1 above basal levels, is provided in isolated and/or purified form.

50. A method according to claim 48 or claim 49 wherein a substance which modulates the ability of Type 1 astrocytes of the ventral mesencephalon, or a molecule or molecules thereof, to induce a dopaminergic fate in neural stem or progenitor cells expressing *Nurr*1 above basal levels, is formulated into a composition comprising one or more additional components.

51. A method according to claim 50 wherein the composition comprises a pharmaceutically acceptable excipient.

52. A method according to claim 51 further comprising administering the composition to an individual.

53. A method according to claim 52 wherein the composition is implanted into the brain of the individual.

54. A method according to claim 53 wherein the individual has

Parkinson's disease.

55. A method according to claim 48 or claim 49 further comprising use of a substance which modulates the ability of Type 1 astrocytes of the ventral mesencephalon, or a molecule or molecules of such astrocytes, to induce a dopaminergic fate in neural stem or progenitor cells expressing *Nurr1* above basal levels, in the manufacture of a medicament for treatment of an individual.

56. A method according to claim 55 wherein the medicament is for implantation into the brain of the individual.

57. A method according to claim 56 wherein the individual has Parkinson's disease.

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